REMARKS/ARGUMENTS

Claims 36-82 are pending. These claims track and find support in the original claim set. Specific support for independent Claim 36 is found in original Claim 1 and on page 4, lines 4 and 13, of the specification which describes SEQ ID NO: 1 and fragments of SEQ ID NO: 1 and on page 4, lines 31-page 5, line 4, which describes sequences which are at least 90-95% identical to SEQ ID NO: 1 and which encode polypeptides with adenosyl homocysteinase activity. Support for independent Claim 69 is found in original Claim 1 and on page 5, lines 8-13, which described polypeptides which are at least 90-95% identical to SEQ ID NO: 2 and which have adenosyl homocysteinase activity. Support for independent Claim 75, directed to sequences which crosshybridize to SEQ ID NO: 1 is found on page 9 of the specification and lines 13-31 describe specific hybridization and washing conditions. Support for Claims 79-81, directed to polynucleotide fragments is found in original Claim 1 and on page 4, lines 21-26, of the specification. Claim 82 finds support in original Claims 20 and 26 and on page 26 of the specification. Accordingly, the Applicants do not believe that any new matter has been added.

New Claims 49-52, 57-60, 65-68, 74 and 78 are process claims, which have been drafted to depend from host cell claims falling within the previously elected Group.

The Applicants thank Examiner Fronda for the courteous and helpful discussion of October 22, 2003. To address the prior art rejections over Pawar et al., it was suggested that the claim set be revised to indicate that the polynucleotide sequences are at least 90-95% identical to SEQ ID NO: 1 or encode polypeptides which are at least 90-95% identical to SEQ ID NO: 2. To help address the enablement and description rejections, the Applicants were advised to describe the claimed polynucleotides using a functional limitation such as "encoding a polypeptide having the adenosyl homocysteinase activity". The deposit rejection could be addressed by perfecting the deposit requirement by making the required statement

regarding continued availability. The Applicants have now made the suggested changes and statement. Accordingly, favorable consideration is now respectfully requested.

Election/Restriction

Group I, directed to polynucleotides, vectors and host cells was previously elected. The Applicants note that the Restriction Requirement has been made FINAL. New Claims 49-52, 57-60, 65-68, 74 and 78 are process claims, which have been drafted to depend from host cell claims falling within the previously elected Group. The Applicants respectfully request that these process claims be rejoined upon an indication of allowability for the underlying product (host cell) claims; see MPEP 821.04.

Rejection—35 U.S.C. §112, first paragraph

Claims 1-3, 5, 6 and 18 were rejected under 35 U.S.C. 112, first paragraph, on two grounds as lacking adequate description or lacking adequate enablement. This rejection is moot in view of the cancellation of these claims. The Applicants respectfully submit that it would not apply to the new claims which are described in terms of a specific functional activity, i.e., "encodes a polypeptide having the enzymatic activity of adenosyl homocysteinase" and structurally, i.e., by reference to "90-95% identity", to specific hybridization conditions or to specific SEQ ID NOS.

Rejection—35 U.S.C. §112, first paragraph

Claim 9 was rejected under 35 U.S.C. 112, first paragraph, as lacking adequate deposit information for the *E. coli* strain deposited as DSM 14316. New Claim 82 corresponds to Claim 9. *Escherichia coli* strain DH5αmcr/pEC-XK99sahHalex was deposited as DSM 14316 under the terms of the Budapest Treaty (see page 21, lines 1-3, of

the specification). As required by 37 C.F.R. 1.808, subject to the one exception permitted by 37 C.F.R. 1.808(b), all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon granting of the patent. See MPEP 2410.01.

Rejection—35 U.S.C. §112, second paragraph

Claims 1-3, 5, 6 and 18 were rejected under 35 U.S.C. 112, second paragraph as being indefinite. These rejections are moot in view of the cancellation of these claims.

Rejection—35 U.S.C. §102(b)

Claim 1 was rejected under 35 U.S.C. 102(b) as being anticipated by Pawar et al., Accession AF262755. This rejection is moot in view of the cancellation of Claim 1 and would not apply to the present claims, such as Claim 36, 69 and 75, which now requires a polynucleotide encoding a polypeptide having adenosyl homocysteinase activity. Pawar is directed to a protein encoding S-adenosyl-L-hydrolase. Claims 79-81 are directed to polynucleotide fragments 30 consecutive nucleotides or longer. The longest match in Pawar appears to be between bases 775-802 (Db) which is only 28 polynucleotides.

Rejection—35 U.S.C. §102(b)

Claim 5 was rejected under 35 U.S.C. 102(b) as being anticipated by Pawar et al., Accession AF262755. This rejection is moot in view of the cancellation of Claim 5 and would not apply to the present claims, such as Claim 75, which now requires a polynucleotide encoding a polypeptide having adenosyl homocysteinase activity and which recites specific hybridization conditions.

Information Disclosure Statement

The information disclosure statement (IDS) filed February 12, 2002 cites documents disclosed in the International Search Report for PCT/EP01/08222. Form 1449 for this IDS considered August 20, 2003 and returned to the Applicants shows the entries for Germany 38 23 451 and Europe 0 435 132 crossed out. English language abstracts for these two documents are provided herewith. Accordingly, the Applicants respectfully request return of a copy of this form showing that these two documents have now been considered.

Allowable Subject Matter

The Applicants thank Examiner Fronda for indicating that the subject matter of Claims 4 and 7, subject to an objection for dependence on a rejected base claim, is otherwise in condition for allowance.

CONCLUSION

In view of the above amendments and remarks, the Applicants respectfully submit that this application is now in condition for allowance. Early notification to that effect is earnestly solicited.

Respectfully submitted,

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AN 112:234001 CA
ED Entered STN: 23 Jun 1990
TI Lysine from recombinant microorganisms
IN Cremer, Josef; Eggeling, Lothar; Sahm, Hermann
PA Kernforschungsanlage Juelich G.m.b.H., Germany; Degussa A.-G.
SO Ger. Offen., 7 pp.
CODEN: GWXXBX
DT Patent
LA German
IC ICM C12N001-21
ICS C12N015-03; C12P013-08; C12P019-34
ICA C07H021-04; C12P019-34; C12P013-08
CC 16-2 (Fermentation and Bioindustrial Chemistry)
Section cross-reference(s): 3
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 3823451	A1	19900118	DE 1988-3823451	19880711 <--
	DE 3823451	C2	19970220		
PRAI	DE 1988-3823451		19880711		

AB The gene for aspartate semialdehyde dehydrogenase (asd) or for dihydropicolinate synthase (dapA) or for both enzymes are cloned in plasmid pZ1k, which is used to transform Corynebacterium glutamicum. The recombinant bacteria are high producers of L-lysine. Thus, the dapA-contg. plasmid pDA3 of E. coli RDA8 and vector pZ1 were both digested with restriction enzymes PstI and SwaI. The vector was treated with phosphatase and the fragments were ligated. The recombinant plasmid pZ1dapt was incubated with protoplasts of C. glutamicum to cause its transformation. The transformed bacteria were cultured at 30.degree. for 72 h with stirring in a medium contg. glucose, (NH4)2SO4, CaCO3, and mineral salts. The lysine concn. in the medium was 41 mM, compared with 33 mM after fermn. with the parent strain.
ST Corynebacterium genetic engineering lysine fermn
IT Corynebacterium glutamicum
(lysine manuf. with recombinant)
IT Fermentation
(lysine, with recombinant Corynebacterium glutamicum)
IT Genetic engineering
(of Corynebacterium glutamicum, for lysine prodn.)
IT Gene and Genetic element, microbial
RL: BIOL (Biological study)
(asd, of Escherichia coli, cloning and expression of, in lysine-producing Cornyebacterium glutamicum)
IT Gene and Genetic element, microbial
RL: BIOL (Biological study)
(dapA, of Escherichia coli, cloning and expression of, in lysine-producing Cornyebacterium glutamicum)
IT 56-87-1P, L-Lysine, preparation
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(manuf. of, with recombinant Corynebacterium glutamicum)

AN 1990-023325 [04] WPIX
DNC C1990-010285
TI Recombinant DNA for increasing lysine prodn. - by Corynebacterium or Brevibacterium, contg. aspartate semi-aldehyde dehydrogenase and/or di hydro di picolinate synthase gene.
DC B05 D16 E16
IN CREMER, J; EGGELING, L; SAHM, H
PA (KERJ) KERNFORSCHUNGSANLAGE JUELICH; (DEGS) DEGUSSA AG; (KERJ) FORSCHUNGSZENTRUM JUELICH GMBH

CYC 1
PI DE 3823451 A 19900118 (199004)* 7p <--
DE 3823451 C2 19970220 (199712) 8p C12N015-03 <--
ADT DE 3823451 A DE 1988-3823451 19880711; DE 3823451 C2 DE 1988-3823451 19880711
PRAI DE 1988-3823451 19880711
IC C12N001-21; C12N015-03; C12P013-08; C12P019-34
ICM C12N015-03
ICS C12N001-21; C12P013-08; C12P019-34
AB DE 3823451 A UPAB: 19930928
New recombinant DNA mols. (I) capable of replication in Corynebacterium or Brevibacterium cells comprise vector DNA (II) and a DNA fragment (III) contg. a gene coding for aspartate semialdehyde dehydrogenase (asd) and/or dihydrodipicolinate synthase (dapA), where (III) is derived from an Escherichia, Serratia or Klebsiella microorganism.

Also claimed are Corynebacterium and Brevibacterium strains contg. (I) and a chromosomal gene coding for L-lysine.

USE/ADVANTAGE - The new strains are useful for fermentative prodn. of L-lysine, giving higher yields than the parent strains from which they are derived.

0/3
FS CPI
FA AB; DCN
MC CPI: B04-B02B1; B04-B04A1; B10-B01B; D05-C01; D05-H04; D05-H12; E10-B01A3

AN 115:90668 CA
ED Entered STN: 06 Sep 1991
TI Lysine manufacture with recombinant Corynebacterium or Brevibacterium
IN Cremer, Josef; Eggeling, Lothar; Sahm, Hermann
PA Forschungszentrum Juelich G.m.b.H., Germany
SO Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DT Patent
LA German
IC ICM C12N015-09
ICS C12P013-08; C07H021-04; C12N001-21
ICI C12P013-08, C12R001-15; C12P013-08, C12R001-13
CC 16-2 (Fermentation and Bioindustrial Chemistry)
Section cross-reference(s): 3, 10
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 435132	A1	19910703	EP 1990-124557	19901218 <--
EP 435132	B1	19940817		
R: BE, DE, FR, GB, IT, NL, SE				
DE 3943117	A1	19910704	DE 1989-3943117	19891227
PRAI DE 1989-3943117		19891227		

AB Lysine manuf. with Corynebacterium or Brevibacterium is made more efficient by introduction of genes for a feedback-insensitive aspartate kinase (I) and for dihydropicolinate synthase. The feedback-insensitive I gene is from a Corynebacterium glutamicum. Expression plasmids based upon the expression vector pJC1 carrying either or both of these genes were prepd. by std. methods and introduced into a C. glutamicum with a feedback-responsive I. Transformants showed a >10-fold increase in the activities. Yields (72 h, 30.degree., glucose/salts medium) of lysine from transformants were from 0 to 50 mM for C. glutamicum 13032 when both genes were introduced (effects were smaller when only one of the genes was introduced). For C. glutamicum DG52-5 the increase was from 43 to 71 mM.

ST lysine manuf recombinant Corynebacterium Brevibacterium; aspartate kinase lysine manuf Corynebacterium; dihydropicolinate synthase lysine manuf Corynebacterium

IT Brevibacterium
Corynebacterium
Corynebacterium glutamicum
(lysine manuf. with recombinant, overexpression of lysine biosynthesis genes in relation to)

IT Fermentation
(lysine, with recombinant Corynebacterium glutamicum)

IT Amino acids, preparation
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(manuf. of, with recombinant Brevibacterium or Corynebacterium)

IT Molecular cloning
(of gene for feedback-resistant aspartate synthase of Corynebacterium glutamicum in Escherichia coli)

IT Plasmid and Episome
(pJC23, dehydropicolinate synthetase gene on, expression in C. glutamicum of, for increased yields in lysine manuf.)

IT Plasmid and Episome
(pJC30, feedback-resistant aspartate kinase gene of Corynebacterium glutamicum on, expression in C. glutamicum of, for increased yields in lysine manuf.)

IT Plasmid and Episome
(pJC50, feedback-resistant aspartate kinase gene of Corynebacterium glutamicum and dihydropicoliate synthase genes on, expression in C. glutamicum of, for increased yields in lysine manuf.)

IT Gene and Genetic element, microbial
RL: BIOL (Biological study)
(lysC, overexpression in Brevibacterium or Corynebacterium of, for increased yields in lysine manuf.)

IT Gene and Genetic element, microbial
RL: BIOL (Biological study)
(dapA, overexpression in Brevibacterium or Corynebacterium of, for increased yields in lysine manuf.)

IT 9012-50-4, Aspartate kinase
RL: BIOL (Biological study)
(feedback-resistant, gene for, overexpression in Corynebacterium glutamicum of, for increased yields in lysine manuf.)

IT 9055-59-8
RL: BIOL (Biological study)
(gene for, overexpression in Corynebacterium glutamicum of, for increased yields in lysine manuf.)

IT 56-87-1, Lysine, biological studies
RL: BIOL (Biological study)
(manuf. with recombinant Brevibacterium or Corynebacterium overexpressing lysine biosynthesis genes)

AN 1991-194725 [27] WPIX
DNC C1991-084237
TI Increasing aminoacid esp. lysine prodn. in Corynebacterium - or Brevibacterium, contg. recombinant DNA with sequences for both di hydro-di picolinate synthase and de-regulated aspartate kinase.
DC B05 D16 E16
IN CREMER, J; EGGELING, L; SAHM, H
PA (KERJ) FORSCHUNGSZENT JUELICH GMBH; (KERJ) FORSCHUNGSZENTRUM JUELICH GMBH
CYC 7
PI EP 435132 A 19910703 (199127)* <--
R: BE DE FR GB IT NL SE
DE 3943117 A 19910704 (199128)

EP 435132 B1 19940817 (199432) DE 11p C12N015-09 <--
R: BE DE FR GB IT NL SE
DE 59006837 G 19940922 (199437) C12N015-09
ADT EP 435132 A EP 1990-124557 19901218; DE 3943117 A DE 1989-3943117 19891227; EP 435132 B1 EP 1990-124557 19901218; DE 59006837 G DE 1990-506837 19901218, EP 1990-124557 19901218
FDT DE 59006837 G Based on EP 435132
PRAI DE 1989-3943117 19891227
REP DE 3823451; EP 143195; EP 197335; EP 219027; EP 387527
IC C07C229-26; C07H021-04; C12N001-21; C12N015-09; C12P013-08; C12R001-15
ICM C12N015-09
ICS C07C229-26; C07H021-04; C12N001-21; C12P013-08; C12R001-15
ICI C12P013-08, C12R001:15; C12P013-08, C12R001:
AB EP 435132 A UPAB: 19930928
Prodn. of amino acid, esp. L-lysine (I), comprises growing a microorganism of the genera Corynebacterium or Brevibacterium which contains recombinant DNA consisting of vector DNA and a sequence for prodn. of proteins with dapA (dihydrodipicolinate synthase) activity, in a nutrient medium, and then recovery of amino acid. The new feature is that the DNA additionally contains a sequence encoding protein with lysC (deregulated aspartate kinase) activity.

Also new are (1) recombinant DNA contg. dapA and lysC sequence plus vector DNA and (2) (I)-producing Corynebacterium and Brevibacterium contg. such DNA.

The DNA coding sequences are esp. derived from a (I)-producing strain, partic. a mutant derived from C. glutamicum ATCC 13032 with reduced feed-back inhibition of aspartate kinase.

USE/ADVANTAGE - Transformants contg. the new recombinant DNA have improved amino acid, esp. (I), secretion rates. They have 15-fold higher dapA and aspartate kinase activities (the rate-controlling factors in (I) biosynthesis).

0/3

FS CPI
FA AB; DCN
MC CPI: B04-B02B1; B04-B04A1; B10-B01B; B11-A; D05-C01; D05-H03B; D05-H04; D05-H12; E10-B01C; E10-B02D